American Journal of Infection Control 42 (2014) 412-6

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

Major article

Prevention of gram-positive infections in peritoneal dialysis patients in Hong Kong: A cost-effectiveness analysis

Carlos Wong BPharm [a], In-wa Luk BPharm [a], Margaret Ip FRCPath, FRCP(Glasg) [b], Joyce H.S. You PharmD, BCPS (Infectious Diseases) [a,*]

[a] School of Pharmacy, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong
[b] Department of Microbiology, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong

Key Words:
Mupirocin
Peritonitis
Exit site infection
Direct medical costs
Quality-adjusted life-years

Background: Gram-positive bacteria are the major causative pathogens of peritonitis and exit site infection in patients undergoing peritoneal dialysis (PD). We investigated the cost-effectiveness of regular application of mupirocin at the exit site in PD recipients from the perspective of health care providers in Hong Kong.

Methods: A decision tree was designed to simulate outcomes of incident PD patients with and without regular application of mupirocin over a 1-year period. Outcome measures included total direct medical costs, quality-adjusted life-years (QALYs) gained, and gram-positive infection–related mortality rate. Model inputs were derived from the literature. Sensitivity analyses evaluated the impact of uncertainty in all model variables.

Results: In a base case analysis, the mupirocin group had a higher expected QALY value (0.6496 vs 0.6456), a lower infection-related mortality rate (0.18% vs 1.64%), and a lower total cost per patient (US $258 vs $1661) compared with the control group. The rate of gram-positive peritonitis without mupirocin and the risk of gram-positive peritonitis with mupirocin were influential factors. In 10,000 Monte Carlo simulations, the mupirocin group had significantly lower associated costs, higher QALYs, and a lower mortality rate 99.9% of the time.

Conclusions: Topical mupirocin appears to be a cost-effective preventive measure against gram-positive infection in incident patients undergoing PD. The cost-effectiveness of mupirocin is affected by the level of infection risk reduction and subject to resistance against mupirocin.

Peritoneal dialysis (PD) is associated with high risk of infection in the peritoneum and at the catheter exit site. Peritonitis increases the risk of hospitalization, prolonged antimicrobial therapy, loss of the dialysis catheter, and mortality.[1,2] Exit site infection (ESI) is a major cause of catheter loss and also contributes to the risk of peritonitis.[3]

Incident PD patients are at greatest risk for ESI and peritonitis within the first year after initiation of PD. In Hong Kong, the mortality rate for patients undergoing PD was 19.1 per 100 patient-years, with infection the most common cause of death.[4] The first 12 months of PD is considered the period of greatest risk for catheter-related infection. Peritonitis occurring during the first year of PD has been identified as an independent factor affecting peritoneal kinetics and duration of survival in PD recipients[5]; thus, preventing peritonitis is crucial to prolonging survival in these patients.

Gram-positive infections account for more than 50% of catheter-related infections, with *Staphylococcus aureus* the most commonly isolated gram-positive pathogen.[3,6,7] In addition, gram-positive infections are highly associated with the first episode of peritonitis in incident PD patients, apparently related to inappropriate connection technique in the newly trained PD recipients.[8] Current recommendations for exit site care include cleansing the exit site with a antiseptic solution (eg, providone iodine, chlorhexidine, hydrogen peroxide, sodium hypochlorite) and sterile gauze. Application of topical antibiotic is suggested, but the adoption of this practice varies among PD care sites. Application of mupirocin ointment at the catheter exit site has been associated with a reduced risk of peritonitis and ESI in PD recipients.[9,10] A cost-effectiveness analysis is essential to facilitate the decision making process of whether to implement regular application of mupirocin

* Address correspondence to Joyce H. S. You, PharmD, BCPS (Infectious Diseases), School of Pharmacy, Faculty of Medicine, The Chinese University of Hong Kong, Shatin, NT, Hong Kong.
E-mail address: joyceyou@cuhk.edu.hk (J.H.S. You).

Conflict of interest: None to report.

0196-6553/$36.00 - Copyright © 2014 by the Association for Professionals in Infection Control and Epidemiology, Inc. Published by Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.ajic.2013.12.008

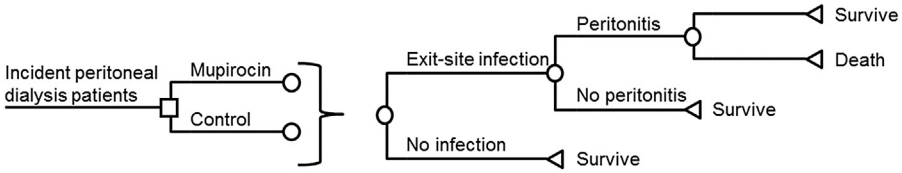

Fig 1. Decision tree.

as a measure to prevent catheter-related infections, particularly in incident PD patients. The present study investigated the potential associated costs, quality of life, and clinical outcomes in incident PD patients with or without regular use of mupirocin from the perspective of health care providers in Hong Kong.

METHODS

Model design

A decision tree was constructed to compare the outcomes of incident PD patients with and without regular application of mupirocin at the PD catheter exit site (Fig 1). The time horizon of the model was the first year of PD, to account for the high-risk duration of PD-related peritonitis and ESI. Three tiers of outcomes were simulated: (1) total direct medical costs, (2) gram-positive infection–related mortality rate, and (3) quality-adjusted life years (QALYs) gained.

In both the mupirocin and control groups, all incident PD patients received routine daily exit site dressing changes. Patients in the mupirocin group applied mupirocin ointment to the exit site once daily at the dressing change. Patients of both groups could develop peritonitis and/or ESI. Those who were infected with peritonitis could subsequently die or survive the infection. Patients infected with ESI alone were assumed to survive.

Clinical inputs

The clinical inputs of the model are listed in Table 1. A MEDLINE literature search for the years 1998-2013 was performed using the following key terms: "peritoneal dialysis," "mupirocin," "gram-positive," "peritonitis," and "exit site infection." The selection criteria for clinical trials were a report written in English, reported prevalence of gram-positive bacteria peritonitis/ESI in PD patients, and reported mortality rate from gram-positive bacteria peritonitis. All articles retrieved by this process were screened for relevance to our model. For variables reported in multiple studies, the weighted average was used to estimate the base case value. The high and low values of the variables reported were tested in sensitivity analyses.

The clinical inputs of the model were estimated from 5 retrospective studies and 1 prospective randomized controlled trial.[3,11-15] The prospective trial examined the difference in the effect on the incidence rates of ESI and peritonitis from local application of mupirocin at the catheter exit site plus routine dressing changes (using chlorhexidine and povidone iodine) versus routine dressing changes alone.[12] Three retrospective studies (2 cohort and 1 case-control) have reported the incidence rates of peritonitis[3,11,13] and ESI,[3,11] and 2 retrospective outcome analyses have characterized peritonitis-associated mortality in PD patients.[14,15]

The weighted average rates (by the sample size of each study) of PD-associated infections, estimated from findings of the 3 retrospective studies (sample sizes 962, 72, and 246)[3,11,13] and the control arm of a prospective trial (sample size 154),[12] were 27.3% (range, 2.5%-38.4%) for peritonitis and 20.2% (range, 2.7%-24.0%) for ESI. The model inputs for rates of PD-associated infections in the mupirocin group were represented by the following equation:

Rate of PD-associated infection × incidence risk ratio (IRR) of PD-associated infection with mupirocin.

Based on the incidence rates of peritonitis in mupirocin group (1/365) and control group (1/40.5) reported in the prospective clinical trial,[12] the unadjusted IRR of gram-positive peritonitis with mupirocin was estimated as 0.11 [(1/365)/(1/40.5)]. The estimated IRR of ESI with mupirocin was 0, given the incidence rates of 0 for the mupirocin group and 1/36.8 for the control group. The model input for mortality rate of peritonitis was the weighted average mortality (5.99%; range, 3.41%-8.94%) from 2 retrospective outcome analyses.[14,15]

Table 1
Model inputs

Input	Base case value	Range for sensitivity analysis	Reference(s)
Clinical inputs			
Gram-positive peritonitis rate, %	27.31	2.47-38.36	3,11-13
IRR after decolonization	0.11	0.088-0.132	12
Gram-positive ESI rate, %	20.17	2.72-23.99	3,11,12
IRR after decolonization	0.00	0.00-0.00	12
Mortality rate of gram-positive peritonitis, %	5.99	3.41-8.94	14,15
Cost inputs, USD*			
Cost of mupirocin (annual)	78	62.4-97.5	Drug cost in Hong Kong
Cost of hospitalization per day	600	—	21
Cost of outpatient specialty clinic visit	142	—	21
Cost of antibiotics for peritonitis treatment per day	1.3	0.38-7	Drug cost in Hong Kong
Cost of antibiotics for ESI treatment, per day	0.2	0.03-0.27	Drug cost in Hong Kong
Length of stay for peritonitis, days	10	7-21	20
Number of clinic visits for ESI	1	1-2	Expert opinion
Length of treatment for peritonitis, days	14	14-21	20
Length of treatment for infection, days	12	10-14	20
Utility inputs			
Incident PD	0.65	0.58-0.88	16-18
Peritonitis	0.19	0.152-0.228	19
ESI	0.58	0.464-0.696	17
Peritonitis-free duration, months	12	1-12	Expert opinion

*1 US$ = 7.8 Hong Kong $.

Utility inputs

The QALYs gained by a patient over the 1-year time period were estimated based on the type of PD-associated infection (if any) experienced by the patient and the utility scores of 4 different health status categories[16-19]: (1) infection-free on PD, (2) PD-associated peritonitis, (3) ESI, and (4) death. To conservatively estimate the additional QALYs gained by topical application of mupirocin, infection and death (if any) were assumed to occur